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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,066	03/23/2007	Erika Jensen-Jarolim	37488.00800US	9617

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	
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06/22/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/562,066	JENSEN-JAROLIM ET AL.
	Examiner	Art Unit
	NORA ROONEY	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4 and 9-19* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4 and 9-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/07/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on 04/05/2011 is acknowleged.

2. Claims 1-2, 4 and 9-19 are pending.

3. Claims 18-19 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 08/23/2010.

4. Applicant's IDS document filed on 10/07/2010 is acknowledged. The items that were crossed out are not publications with publication dates, thought they have been considered.

5. Claims 1-2, 4 and 9-17 are currently under consideration as they read on microspheres containing antigens and/or DNA of antigens, wherein the microspheres comprise the *Aleuria aurantia* lectin on the surface and wherein the microspheres have a binding constant KB of at least 1 x 10^4 M^1 toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells.

6. In view of Applicant's amendment on 04/05/2011, only the following rejections are maintained.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-2, 4 and 9-17 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: PLGA microspheres containing birch pollen extract wherein the microspheres have lectins on their surface; does not reasonably provide enablement

for: **microspheres containing antigens and/or DNA of antigens, wherein the microspheres comprise the *Aleuria aurantia* lectin on the surface** and wherein the microspheres have a binding constant KB of at least 1 x 10^4 M^1 toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells of claim 1; **wherein the specific carbohydrate residues is alpha-L-fucose** of claim 4; **wherein the antigens and/or DNA of antigens are allergens and/or DNA of allergens** of claim 16; **wherein the antigens are mimotopes of the allergen Phl p 5 and/or of the allergen Bet v 1** of claim 17 and as applied to claims 4 and 9-15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claims for the same reasons as set forth in the Office Action mailed on 10/06/2010.

Applicant's arguments filed on 04/05/2011 have been fully considered, but are not persuasive.

Applicant argues:

> "This rejection is respectfully traversed. The Examiner appears to be basing a significant part of the rejection on the content of the microspheres. In other words, the Examiner contends that the specification has to enable a representative number of antigens that could be contained in the microspheres *and show an immune response*. However, the claims cover a product, *i.e.,* microspheres, and not a method. By this amendment, the term "for allergy therapy" has been deleted from the claim. The invention is microspheres having a certain binding constant based on surface properties, then it is irrelevant what the microspheres contain. The microspheres can theoretically contain *any* therapeutic suitable for the microsphere environment and this should not be subject to an enablement rejection for composition of matter claims.

It is the Examiner's position that the claims are directed to a product—a product that has to be able to be made and used with guidance in the specification. In addition, even though "for allergy therapy" has been deleted, the recited microspheres also "have a binding constant K_B of at

least 1 x 10^4 M^{-1} toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells." The specification has not adequately disclosed the genus of microspheres with a binding constant K_B of at least 1 x 10^4 M^{-1} toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells and which can be made and used according to the guidance in the specification.

Brayden et al. (PTO-892; Reference U) teaches that *Ulex europaeus* agglutinin 1 (UEA-1) has high specificity for α-L-fucose, located on the apical membranes of mouse M cells. There have been successful efforts made into *in vivo* targeting to mouse M cells by conjugating the lectin to polymerized liposomes and also to latex particles. Other studies orally vaccinated mice with latex particles coated with albumin and UEA-1 inducing an enhanced level of serum IgG and IgM compared to untargeted BSA-coated particles. The reference teaches that UEA-1 is of limited value in vaccine delivery because the lectin is toxic, is subject to intestinal degradation, and its receptor is not expressed in human Peyer's patches and not even by all murine M cells. Brayden also teaches that while stable non-toxic small molecule mimetics of lectins could have potential in oral vaccine targeting, demonstration of reproducible receptor expression in human Peyer's patches is a prerequisite. On page 1150 the reference states "The edible orange peel mushroom *Aleuria aurantia* was used to target the α-L-fucose receptor. Coated poly(D,L-lactide-co-glycolide) (PLG) particles were entrapped with birch pollen antigens and administered to mice as a potential oral allergen immunotherapy [52]. In pollen-sensitized mice, oral administration of this formulation led to increases in interferon-γ and IgG2a antibody. Convincing demonstrations that antigen-loaded M-cell fucose receptor targeted biocompatible particles can genuinely enhance systemic and mucosal immunity in mice would provide a

stronger case to support the linkage between targeting and vaccine efficacy. However, human M-cells are unlikely to show specific UEA-1 lectin binding and it will be interesting to see if regulatory authorities will permit human Phase I testing of a UEA-mimetic with an antigen loaded particle, even if murine immune data has turned out to be positive [53]." Therefore, the post dated art is unconvinced of the efficacy of the Aleuria aurantia lectin for vaccine efficacy in mice, much less in humans which do not express α-L-fucose on their surface.

The post-dated art of Azizi et al. (PTO-892; Reference V) also teaches that lectin-binding studies in experimental animals have shown that M cells express on their surface a particular glycosylation pattern. Studies showed that Ulex europaeus agglutinin-1 (UEA-1), a lectin specific for a-l-fucose residues, selectively binds to M cells in murine Peyer's patches. However, M cell glycosylation patterns are not common to all species, and it remains to be seen whether it can be used to effectively target human M cells. Human M cells have proven to be largely anonymous, as it has been difficult to isolate enough of such cells for further characterization and functional evaluation. Therefore, the specific receptor requirements for human M cells and how to specifically target these receptors remains a challenge (In particular, page 4, left paragraph, whole document).

The specification does not disclose the genus of antigens that can be bound to microspheres that will result in having a binding constant K_B of at least 1×10^4 M^{-1} toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells and which can be used according to the disclosure in the specification for treatments. The art shows that human

intestinal cells do not possess specific carbohydrates for the recited binding, though the claims read on human intestinal and epithelial cells.

Therefore, the art does not show and the specification does not teach the genus of microspheres with a binding constant K_B of at least 1 x 10^4 M^{-1} toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells and which can be made and used for therapies disclosed in the specification. As such, the rejection is maintained.

9. Claims 1-2, 4 and 9-17 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons as set forth in the Office Action mailed on 10/06/2010.

Applicant's arguments filed on 04/05/2011 have been fully considered, but are not found persuasive.

Applicant argues:

> "Again, the Examiner's reference to the allergen in the microsphere is irrelevant. Further, by this amendment, claim 1 is amended to recite that the microspheres contain the *Aleuria aurantia* lectin on the surface. Support for this amendment is found in the specification at e.g., paragraph 23-28 on pages 5-6. Because the specification clearly describes microspheres containing the *Aleuria aurantia* lectin that have a binding constant of at least 1 x 10^4 M^{-1} toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells, this claim is sufficiently described. There is a specifically disclosed correlation between the structure of the microspheres expressing the claimed lectin *(Aleuria aurantia)* and the property of the binding constant."

Characterization of the recited microspheres is part of the invention and until it has been done the claimed invention is not adequately described. The specification does not disclose a correlation between the structure of the microspheres comprising antigens and their function (with a binding constant K_B of at least 1 x 10^4 M^{-1} toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells) and which can be used for therapeutic purposes as described in the specification such that a skilled artisan would have known what microspheres possess the claimed functions. "Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features" *Ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)), at page 16. In this instant case, Applicants have not provided the requisite identifying structural features of the microspheres with antigens encompassed that will result in the claimed function of having a binding constant K_B of at least 1 x 10^4 M^{-1} toward the specific carbohydrate residue of intestinal and/or nasal epithelial cells. "Without a correlation between structure and function, the claim does little more than define the claimed invention by function" *supra,* at page 17. Definition by function does not suffice to define the genus because it is only an indication of what the peptides do, rather than what they are.

Therefore the rejection is maintained.

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

June 17, 2011

/Nora M Rooney/

Primary Examiner, Art Unit 1644